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09/837,138	04/18/2001	John H.J. Petrini	800.019US3	9954

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	12

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/837,138	Applicant(s) Petrini et al
	Examiner Karen Canella	Art Unit 1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *5, 6, 16-18, and 20-27* is/are pending in the application.

4a) Of the above, claim(s) *16-18 and 23-25* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *5, 6, 20-22, 26, and 27* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Apr 18, 2001* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of Group I drawn to methods of altering the amount of a DNA repair polypeptide in a cell comprising the recombinant expression of a nucleic acid molecule, and transformed host cells prepared thereby, classified in class 435, subclasses 69.1 and 325. The traversal is on the grounds that the inventions are so closely related that they cannot be properly considered independent and distinct within the statutory meaning of 35 U.S.C. 121 and that in particular, claims drawn to a transgenic mouse comprising a nucleic acid segment encoding a DNA repair polypeptide, and claims drawn to a method of using the transgenic mice to screen for agents which modulate a DNA repair polypeptide, should be included with the instant invention. This has been considered but not found persuasive. Inventions drawn to transgenic mice and methods of using said mice have completely different issues regarding enablement under 35 U.S.C. 112, first paragraph in comparison to methods drawn to recombinant expression in an isolated cell because isolated recombinant cells are made by completely different methods than transgenic mice. As to the question of burden of search, the claims of Groups II and III are classified differently, necessitating different searches in the U.S. Patent shoes. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Clearly different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

2. Claims 5, 6, 16-18 and 20-27 are pending. Claims 16-18 and 23-25, drawn to non-elected inventions, are withdrawn from consideration. Claims 5, 6, 20-22, 26 and 27 are examined on the merits.

Claim Objections

3. Claims 20 and 21 are objected to as being dependent upon a non-elected invention as claim 17 is withdrawn from consideration.

Claim Rejections - 35 USC § 112

4.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5, 6, 20-22, 26 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 are vague and indefinite in the recitation of "biologically active fragment thereof". The specification provides no definition or standard with which to ascertain the difference between a "biologically active fragment" and a "fragment", as no specific biological activity has been contemplated by the specification to limit the metes and bounds of "fragment thereof" . Thus it is unclear how "biologically active" further limits the methods relying on the claimed fragments.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 5, 6, 22, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for full length DNA repair proteins, does not reasonably provide enablement for biological fragments thereof. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of 35 U.S.C. 112 states that "the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...". The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation. The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ (CCPA 1977)). Additionally the courts have determined that "...where a statement is , on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971)). Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph have been described in In re Colianni, 195 USPQ 150, 153 (CCPA 1977) and have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986). Among the factor are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

Claims 5 and 6 are drawn in part to a method reliant upon a biologically active fragment of a DNA repair polypeptide.

The art teaches that the function of a single DNA repair protein is complex as it interacts with numerous cellular proteins. For instance, the instant claims read on methods of expressing XPB and XPD, for the reasons set forth in the art rejections below. However, it is recognized in

the art that XPB and XPD interact with each other in addition to p44, p62, TTDA, p34, XPA, and ERCC1 and that DNA repair proteins often have dual roles such as XPB and XPD which are involved in transcription as well as DNA repair (for instance see Thompson in: DNA Damage and Repair, (monograph) Vol. 2, 1998, pages 335-393, Nickoloff and Hoekstra, Eds, especially p. 351, fig. 2 and section 3.3.2, "Repair Proteins as Transcription Factors-dual Roles", page 355).:

The specification merely contemplates that "biologically active fragments" are part of the claimed invention, not instructions limiting the type of biological activity, guidance with respect to specific protein domains nor have any working examples have been set forth.

The claims are broadly drawn to methods of altering the amount of a DNA repair polypeptide in a cell by the expression of an isolated nucleic acid encoding, or antisense to, a biologically active fragment of a DNA repair polypeptide having a molecular weight of about 95 kDa. When given the broadest reasonable interpretation, the claims encompass any fragment of said DNA repair polypeptide, and the specification is lacking in teachings of how to make said fragments, as no criteria have been set forth about specific proteins domains, and the specification is also lacking in teachings of how to use the broadly claimed invention, which would express a partial DNA repair polypeptide, the activity of which would be unknown. Given these lack of teachings and the unreliability of the art with respect to the complexity of interactions between DNA repair polypeptides and other cellular proteins, one of skilll in the art would be subject to undue experimentation in order to make and use the broadly claimed invention.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

9. Claims 5, 22, 26 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Kowalski (WO 98/07030) as evidenced by Nickoloff and Hoekstra (DNA Damage and Repair, (monograph) Vol. 2, 1998, pages 348-349). Claim 5 is drawn to a method of altering the amount of a DNA repair polypeptide in a cell comprising introducing into the host cell an isolated nucleic acid molecule comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a molecular weight of about 95 kDa or a biologically active fragment thereof operable linked to a promoter functional in the host cell so as to yield a transformed host cell; and expressing the nucleic acid molecule in the transformed host cell a recombinant DNA repair polypeptide, wherein the amount of the recombinant polypeptide produced by the transformed cell is different than the amount of the DNA repair polypeptide produced from the corresponding non-transformed cell. Claim 22 embodies the method of claim 5 wherein the host cell is a mammalian cell. Claim 26 is drawn to the transformed host cell prepared by the method of claim 5. Claim 27 embodies the host cell of claim 26 wherein said cell is a mammalian cell.

Kowalski discloses a method for altering the amount of a DNA repair polypeptide in a cell comprising introducing into the host cell an isolated nucleic acid molecule encoding the XPB or XPD polypeptides (page 12, lines 6-21, page 15, lines 20 to page 16, line 7). Kowlaski discloses that the host cell is preferably a mammalian cell. Kowlaski contemplates that the recombinant molecule can induce, enhance, delete activity of the protective cellular mechanism. Nickoloff and

Hoekstra disclose XPB and XPD as DNA repair proteins having a molecular weight of 89 and 87 kDa, respectively, which fulfills the specific embodiment of "about" 95 kDa.

10. Claims 6 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Housman et al (WO 98/41648) as evidenced by Nickoloff and Hoekstra (DNA Damage and Repair, (monograph) Vol. 2, 1998, pages 348-349).. Claim 6 is drawn to a method of altering the amount of a DNA repair polypeptide in a cell comprising introducing into a host cell comprising the complement of at least a portion of a nucleic acid molecule comprising a nucleic acid segment encoding a vertebrate DNA repair polypeptide having a molecular weight of about 69 kDa or a biologically active fragment thereof operably linked to a promoter functional in the host cell so as to yield a transformed cell; and expressing the DNA segment in the transformed host cell as antisense RNA so as to decrease the amount of the DNA repair polypeptide in the transformed cell. Claim 22 embodies the method of claim 6 wherein the host cell is a mammalian cell.

Housman et al disclose a methods for altering the amount of DNA repair polypeptide in a cell comprising the administration of antisense oligonucleotides to patients (page 46, line 21 to page 47, line 22 and page 381, claim 119). Housman et al identifies ERCC2 and ERCC4 as target genes for said therapy (page 385, claim 129). Nickoloff and Hoekstra identify ERCC2 and ERCC4 as DNA repair proteins having a molecular weight of 87 and 104 kDa, respectively, thus fulfilling the specific embodiment of "about" 95 kDa. Further, it would be inherent in the method of Housman et al that the host cell is a mammalian cell.

11. Claims 5 and 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Camonis et al (U.S. 6,479,237) as evidenced by Nickoloff and Hoekstra (DNA Damage and Repair, (monograph) Vol. 2, 1998, pages 348-349).

Camonis et al disclose a method for detecting or identifying protein involved in the formation of a protein complex comprising the expression of the XPB or XPD proteins fused to

the VP16 protein (column 12, line 65 to column 13, line 4) in yeast cells as host cells. It would be inherent in the method of Camonis et al that the method altered the amount of DNA repair polypeptide in the cell. Nickoloff and Hoekstra disclose XPB and XPD as DNA repair proteins having a molecular weight of 89 and 87 kDa, respectively, which fulfills the specific embodiment of "about" 95 kDa.

12. All claims are rejected.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

February 24, 2003